

The Chronic Critically Ill: Pulmonary Perspective

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Introduction

Within the past decade there have been a number of large scale pivotal clinical trials in critically ill patients evaluating a variety of treatment modality comparisons which have generated contemporary robust data in relation to acute intensive care unit (ICU) mortality. Reported values for 28-day to 90-day mortality for various designated populations of ICU patients include: a) general ICU population of patients: 11-28% [1,2]; b) patients with all-cause shock: 17-53% [3-5]; c) patients with sepsis and septic shock: 36-54% [6-8]; d) patients with acute respiratory distress syndrome (ARDS)/acute lung injury (ALI) diagnosed by study specific definitions which severity were determined based upon the ratio of partial pressure of arterial oxygen (PaO₂) to the fraction of inspired oxygen (FiO₂): 22-47% [9-12].

The converse of this mortality data is that dependent upon specific disease and organ systems failure approximately 50 to 90% of ICU patients survive their critical illness. However, buried in this population of short-term (less than 90 days) ICU survivors is a unique and distinct cohort of patients, termed the “chronic critically ill” (CCI) whose long term survival and return to independent functional status remain abysmal. The purpose of this publication is to highlight recent observations in relation to the identification, epidemiology, outcomes, and potential preventive strategies for CCI patients. Our intent is not only to raise awareness but also to propose some recommendations to stimulate and encourage actions towards methods for improvements in care, management, and clinically relevant patient outcome measures.

Methods

Data was extracted by a non-structured, random review of selected relevant manuscripts from multiple publication sources including but not limited to medical, surgical, critical care, nursing, and health policy peer-reviewed journals. Given a) the common requirement for prolonged mechanical ventilation (PMV) in the current working definition and diagnosis of CCI patients and b) the current understanding of this unique post-ICU syndrome, emphasis for literature review was appropriately weighted upon potential mechanism and contributing causes of PMV.

Definition

The populations of CCI patients are not easy to recognize even when one considers their severe burden of acute disease, pre-morbid concomitant disease and functional status, and potential requirement for prolonged mechanical ventilation (PMV). Multiple definitions of the CCI patient exist focusing primarily on ventilation status. Such definitions include a) defining onset of CCI at the point where

tracheostomy is performed in anticipation of need for PMV, or b) defining onset of CCI based solely upon a specific duration of mechanical ventilation (MV) such as between 7–21 days [13]. From a clinical perspective a definition of CCI based upon the development of tracheostomy and prolonged mechanical ventilatory support is a simple universal definition. However, such a respiratory based definition or priority ignores the inter-dependence of multi-system abnormalities that often create the necessity of PMV including other mechanical support modalities such as dialysis, altered mental status, delirium, confusion, malnutrition, muscle atrophy, de-conditioning, and ICU acquired weakness (ICU-AW). Although PMV is the hallmark of this CCI syndrome, it is clearly not sufficient by itself to characterize this distinct ICU patient population [14,15]. Additional limitations of over-emphasis upon ventilator status also include a) the fact that most cases of PMV although perhaps initiated by intrinsic lung disease, rarely is the necessity for PMV maintained by primary lung disease but rather perpetuated by non-lung factors and b) the concept that time should not be the sole additional defining variable. In addition, as per current definition PMV is a necessary but not sufficient component to define the syndrome of CCI since not all patients who require tracheostomy and PMV will evolve into this syndrome. Such patients include those with neuromuscular disorders that severely compromise ventilatory status including Guillain-Barre syndrome, acute cervical spinal cord injury, or amyotrophic lateral sclerosis.

With this information as background, it is perhaps best to think of patients with CCI as composed of multiple debilitating physiological abnormalities including a) profound muscular weakness both locomotor and respiratory, b) extreme alterations in body composition such as loss of lean body mass, increased adiposity, or anasarca, c) neuroendocrine disorders, d) immunological deficits with associated increased vulnerability to infections (defined as immune exhaustion) often with highly virulent and drug resistant hospital-derived pathogens, [16] e) skin breakdown and decubitus ulcers, f) malnutrition, g) prolonged immobility and de-conditioning, h) stool and urinary incontinence, and i) multiple varieties of brain dysfunction including delirium and coma [17]. Thus CCI is not simply a prolongation of acute illness but represents a distinct post-acute illness syndrome of physiological and pathological abnormalities with PMV simply serving as a “starting point” [18]. As stated previously as research continues to advance our knowledge of the CCI patient this limited definition will clearly expand and evolve.

Epidemiology

The impact of the changing epidemiology of the CCI patient population is evident from a variety of perspectives; a) CCI patient volumes, b) CCI patient resource utilization, c) CCI patient acute and

long term clinical outcomes, and d) CCI patient mortality. Numerous studies have established the changing population-based characteristics of the ICU patient population from multiple perspectives; a) expanding overall numbers and volumes of ICU patients, b) increasing age of the elderly ICU population, c) improved overall survival, d) explosion of scientific and technological advancements to prolong life and mechanically support failed organs for indefinite durations, and e) the expectation of all patients to receive ICU quality care if the need arises. As a result or as a consequence of these changing ICU population characteristics, the population of CCI patients has dramatically risen and will continue to expand for the foreseeable future. Estimates suggest that between 5-20% of all mechanically ventilated ICU patients will progress to PMV [19]. Using data for the year 2000 from the National Inpatient Sample (NIS) developed by the Agency for Healthcare Research and Quality and discharge diagnostic codes for year 2003 approximately 300,000 hospital discharges during that period of time in the U.S.A. involved patients requiring PMV; for the year 2005 approximately 400,000 PMV patients and projected estimates for 2020 thought to exceed 600,000 PMV patients [20,21]. Although the CCI account for only 10% of all ICU patients receiving MV, they tend to consume 20-40% of ICU bed days and critical care resource utilization [17]. In addition estimates suggest that over 50% of the total time patients are receiving invasive mechanical ventilation is devoted solely to the ventilator weaning and liberation process.

Mortality rates at 28 days for all patients receiving mechanical ventilation in the ICU setting for years 1998, 2004, and 2010 were reported as 33%, 32%, and 30% respectively [22]. In one large study of 6,469,674 total hospitalized patients reported from 6 states in 2005, 180,326 (2.8%) required any duration of invasive mechanical ventilation. This subpopulation of 180,326 patients had an in-hospital mortality of 35% and only 30% were eventually discharged to home [23]. Notably, the development of PMV appears to represent a marker of even higher mortality risk with rates reported at 3, 6, and 12 months measuring 41%, 46%, and 63% respectively. In addition the category of PMV patients aged 75 years and older manifest an even greater one year mortality rate approaching 75% [24,25].

Poor clinical outcomes in the PMV patient with CCI are not only resultant from the reported elevated mortality rates but also poor functional, physical, mental, and psychological recovery [26]. In one study of 334 patients who a) required mechanical ventilation beyond 72 hours during their ICU stay and b) survived their acute hospitalization; 277 patients were eventually discharged not ventilator dependent but 57 were discharged still dependent upon full mechanical ventilatory support [27]. Defining a "better" outcome based upon criteria of both a) alive at 4 months and b) without cognitive impairment at 2 months; for the population discharged not-ventilator dependent equal numbers were defined as having either "better" or "worse" outcomes. However for the 57 patients discharged on mechanical ventilation, only 1 patient (2.5%) satisfied the above definition of a "better" outcome [27].

Multiple additional studies have again corroborated the spectrum of poor overall recovery (medical, functional, physical, emotional, and psychological) in this select cohort of patients with CCI. In a single institution study of 126 patients who met conventional definition of PMV, i.e. either greater than 21 days on full MV or requiring placement of tracheostomy for PMV, outcome assessments demonstrated that at one year follow-up, 70 (56%) were alive, but only 11 (9%) were alive with no functional dependency and only 19 (27%) were perceived as having a "good" quality of life [28]. In another

separate published study of 385 patients defining CCI as onset of tracheostomy in anticipation of PMV, at 6 months after discharge or transfer from an acute care hospital 48% were successfully weaned and liberated from MV, 56% died either during index hospitalization or at the transfer facility, but again only 14% returned home and only 15% were alive without long-term brain dysfunction (LTBD) [29].

Identifiable Risk Factors and Conditions

Risk Identification

Acknowledging a large population of ICU patients at risk for development of CCI, the question arises as to the ability to predict or at least identify these patients prior to requirement for PMV and CCI progression. Again focusing upon the current requirement for PMV in definition of CCI, studies have shown that even experienced intensivists and critical care physicians have low predictive accuracies of only 37% in estimating the duration of MV based upon predictive assessment at the time of MV initiation with predictions under and over estimation of actual duration of MV in 33% and 30% of cases, respectively [30]. Perhaps this lack of predictive accuracy might reflect the over-emphasis upon the lung per se and the specific lung disease precipitating acute respiratory failure rather than focusing on the entire respiratory system and the clear evidence that respiratory muscle dysfunction or insufficiency and acute brain dysfunction remain main contributors to PMV [31,32]. With this as background, emphasis would seem most appropriately directed towards two systems abnormalities with direct negative impact upon respiratory status and the potential progression from MV to PMV in attempts to arrest the development of CCI; a) skeletal muscle dysfunction most importantly the diaphragm and b) abnormalities of mental status, cognitive function, and acute brain dysfunction (including medication-induced) [33].

ICU-Acquired Weakness (ICU-AW)

ICU-AW is not the result of a single disease but rather the overall consequence of multiple injurious agents to the skeletal muscles both locomotive and respiratory. Usually the degree of skeletal muscle weakness is perceived as less important during early ICU stay than later when manifested as failure to wean or severe functional deficits during the rehabilitation period [34]. ICU-AW should be regarded as an equally important component of critical illness multi-organ failure (MOF) with the caveat that improvement of muscle weakness often lags behind the degree of recovery in other failed organs both in magnitude and duration. This significantly impacts the overall recovery and rehabilitation process since CCI patients then begin recovery with markedly reduced muscle reserves. Factors contributing to ICU-AW include a) the pre-morbid overall health status of the patients in relation to malnutrition, obesity, de-conditioning, and reduced exercise capacity; b) direct insults to the neuromuscular system and the resultant consequences upon skeletal muscle function including drugs, critical illness polyneuropathy (CIP) and critical illness myopathy (CIM), inflammation, rhabdomyolysis, and the unique identification of ubiquitin-mediated protease lysis of diaphragmatic muscle protein components necessary for contractile function, and c) indirect influences such as immobility and disuse atrophy [35].

CIP is primarily the result of neuronal axonal degeneration typically affecting motor nerves more than sensory nerves whereby demyelination is usually not typical [36,37]. CIM is an acute primary

myopathy with histological changes consisting of muscle fiber atrophy, selective loss of myosin filaments, variable degrees of myofiber necrosis and regeneration [38]. Major clinical features of CIP/CIM are flaccid weakness that is often missed because of acute illness, encephalopathy, and sedating drugs.

Prolonged inactivity and immobility, especially in association with systemic inflammation as seen in cases of sepsis, septic shock, and systemic inflammatory response syndrome (SIRS) also create abnormalities in muscle metabolism. When looked for aggressively, reported incidence of immobility-induced muscle weakness approaches 25% at 7 days [35]. If including the diagnosis of sepsis and multi-organ failure the incidence increases to over 50%. These abnormalities are often cortisol-mediated and result in loss of both muscle and lean body mass [39]. Healthy young volunteers exposed to 28 days of bed rest experienced 0.4 kg loss of lean leg mass that was amplified into a 23% reduction in leg extensor strength and function [39]. In a companion study similar healthy young volunteers were again exposed to bed rest but in association with exogenous daily hydrocortisone administration which effected an exaggerated 1.4 kg or 0.6% loss of lean body mass that again resulted in a marked amplification of resultant physiological functional deficit as evidenced by a 30% reduction in leg extensor strength [39].

For comparison with the critical care setting, during illness imposed bed rest the greatest loss of lean tissue occurs in skeletal muscle with studies showing muscle fiber area decrease by 1-4% per day in the ICU [39-41]. The loss of lean body mass during ICU stay of between 1-4% per day is far greater than would be expected from immobilization alone [41]. Similar ventilator-induced diaphragmatic disuse atrophy is also thought to be a contributing factor to respiratory muscle weakness, dysfunction, loss of force generating capacity and the resultant perpetuation of the necessity for PMV.

In all individuals, healthy muscle mass is dynamically maintained through a balance of skeletal muscle protein synthesis exceeding protein breakdown [40]. For muscle wasting to occur, especially in CCI patients this system is imbalanced with degradation exceeding synthesis which imbalance is not corrected by nutritional repletion or supplementation [42]. Thus any efforts directed to treatment of ICU-AW must also include the ability to halt the protein destructive process and enhance amino acid uptake and utilization by the metabolizing skeletal muscle to promote synthesis; again noting the observation that total body protein synthesis is less responsive to the effects of amino-acid and nutritional supplementation during critical illness. In a limited ICU study of five patients who were receiving continuous neuromuscular pharmacological blockade for 7 days, the utilization of a mechanical continuous passive motion device demonstrated preservation of muscle fiber mass and protein content in 3 out of 5 patients in the active motion leg compared to significant muscle wasting in the contra-lateral control leg [43]. In a more recent study of a small cohort of 20 acutely ill patients admitted with coma secondary to either traumatic brain injury or stroke and who remained immobilized a minimum of 7 days (14 in the intervention group and 6 in the control group), the application of electrical muscle stimulation (EMS) demonstrated preservation of muscle mass as assessed by weekly computerized tomography (CT) scans of various lower extremity muscle compartments following 30 minute daily EMS for a protracted duration of 35 days [44]. Although not specifically evaluated in the select cohort neither of CCI patients nor in relation to diaphragmatic muscle weakness, these physical therapy-directed interventions merit potential expanded investigation.

Since PMV is a hallmark of CCI it is most appropriate to focus specifically upon the respiratory muscles and their loss of strength and endurance capacity as perhaps the most significant contributing factor to requirement for PMV. Clinical studies have consistently demonstrated that in absence of drug-induced sedation and in the absence of primary neurological injury or disease, a) the central nervous system (CNS) drive to maintain ventilation is well preserved and often exaggerated in patients receiving PMV; b) dependent upon the particular individual patient, the mechanical work of breathing (WOB) may be either increased (such as acute exacerbation of severe COPD) or normal (such as resolved ARDS or acute pneumonia;) but c) consistently all patients have demonstrated severe reductions in diaphragmatic strength and endurance below the threshold necessary to maintain sustained spontaneous ventilation [45]. In a classic study, acknowledging the potential contribution of ventilator-induced diaphragmatic disuse atrophy, Levine et al studied the histology and metabolic parameters of diaphragm muscle biopsies from a) control ICU patients who received MV for durations of 2-3 hours and b) brain dead patients in the absence of any diaphragmatic neural activation or active muscle contraction who received MV for durations ranging from 18-69 hours [46]. This study demonstrated and subsequently was corroborated by other investigators [47,48] that brain dead patients manifested a mean 57% decrease in cross sectional area of slow-twitch fibers and mean 53% decrease in cross sectional area of fast-twitch fibers when compared to controls. In addition, biochemical analyses of these same specimens clearly demonstrated activation of excess of caspase-mediated muscle fiber proteolysis as a contributing factor to correlate with the histological examinations, caspase being a protease enzyme involved in the initial steps of muscle fiber proteolysis. Thus similar to the multi-factorial causality of ICU-AW, the diaphragm appears to also have an additional unique susceptibility to actual enzymatic destruction of muscle fibers contributing to overall muscular effectors dysfunction, profound weakness and perpetuation of the necessity for PMV, in addition to ventilator-induced diaphragm muscle fiber atrophy.

Immobility and Deconditioning

Acknowledging the impact of ICU-AW upon both acute liberation from mechanical ventilation and long-term functional status and rehabilitation potential, there is an abundance of accumulating evidence supporting the benefits and safety of early mobilization in the ICU of critically ill patients even those receiving invasive MV. One such study demonstrated that in an early intervention mobilization cohort of critically ill patients immediate outcomes benefit included a) reduced number of ICU delirium days (2 days vs. 4 days), b) reduced time in ICU with delirium (33% vs. 57%), and c) reduced duration of mechanical ventilation (3.4 days vs. 6.1 days) [49]. However overall hospital mortality was similar (18% vs. 25%) but importantly long term recovery and return to independent functional status at hospital discharge was also clearly improved [49]. Evidence is emerging that early mobilization may mitigate the development and/or duration of ICU-AW and should be initiated before profound atrophy, deconditioning, debility and malnutrition develop. In one study early intervention efforts were successful in achieving a number of remarkable milestones in mechanically ventilated and intubated patients: 76% achieved bed mobility and legs dangling between 1-2 days; 33% achieved standing and weight bearing at mean 3.2 days; and 15% achieved full ambulation at mean of 4 days [37,50]. Because physical function is closely associated with quality of life, maintaining even a minimal level of residual physical activity is essential in

promoting and maintaining a sense of well-being [15]. Physiotherapy should be given early priority in ICU care and specifically educated physiotherapists should be included as an important component of the multi-disciplinary ICU team [51]. Standardized protocols of early mobilization, physical therapy, and cognitive rehabilitation should be instituted within all ICUs similar to current protocol based practices of spontaneous breathing trials, vasopressor titration, and blood glucose monitoring [37,49-51].

Delirium

Using two validated delirium screening tools, the intensive care delirium screening checklist (ICDSC) and the confusion assessment method adapted for the ICU (CAM-ICU), reported frequencies of ICU delirium ranging from 16-45% and 30-89% respectively [52]. Delirium has consistently been identified as a negative prognostic indicator in relation to multiple ICU outcomes including duration of mechanical ventilation, length of hospitalization, and nosocomial complications [53,54]. In addition there is a strong association between the number of ICU days with delirium and mortality. Although durations of ICU delirium may appear relatively short as measured in days, survivors may have protracted neurocognitive impairment for chronic long term durations measured in months and years. Rarely is delirium in the critically ill patient caused by a single factor, rather it is a multi-factorial syndrome resulting from an imbalanced interaction of individual patient vulnerability in the presence of overwhelming predisposing insults [55]. Important identifiable delirium-predisposing risk factors include a) baseline cognitive impairment, b) sleep deprivation, c) immobility, d) visual impairment, e) hearing impairment, f) dehydration and g) drugs and medications [52,55]. Medications are perhaps the most prevalent modifiable risk factor for prevention of ICU delirium. Most importantly, increasing doses of benzodiazepines have been shown to increase the risk of ICU delirium in a dose-dependent fashion [52,53]. Once delirium is overt, other therapeutic interventions to treat delirium have marginal proven efficacy. Despite guideline recommendations, there are currently no drugs with regulatory approval for the treatment of ICU delirium. Thus primary prevention of delirium onset is the most effective strategy.

Neuropsychiatric Abnormalities

The burden of poor health status in ICU surviving CCI patients is not just functional or physical, between 25-75% of survivors of acute ICU illness manifest deficits in memory, attention, concentration, global intellect, and mental processing. In one published study rates of neuropsychiatric deficits included: a) anxiety 63/102 (62%), b) cognitive impairment 41/75 (55%), c) poor executive function 37/76 (49%), d) post-traumatic stress disorder (PTSD) 40/102 (39%), e) depression 37/102 (36%), f) difficulty with verbal fluency 15/96 (16%), and g) memory impairment 12/92 (13%) [56]. Similar neuropsychiatric deficits plus significant functional disability and perceived reduced quality of life (QOL) have also been observed in survivors of ARDS which encompassed a relatively young aged population of critical ill patients with mean age of approximately 45 - 50 years [56,57]. In one published study of ARDS survivors 75% of patients had multiple cognitive defects at one year and only 75% returned back to work at five years post recovery [57]. In a recent publication of one year follow-up of 821 total patients, both medical and surgical, who survived their ICU stay, 24% exhibited cognitive impairment of some degree at 1 year to a magnitude by objective

intelligence/mental testing similar in severity to patients with mild Alzheimer's disease and 34% manifested cognitive impairment typically associated with moderate traumatic brain injury [58]. Thus cognitive rehabilitation must also begin early in the course of ICU care and be considered an important objective of both acute and chronic care plans [59]. In a well regulated study that longitudinally evaluated 186 survivors of ARDS that utilized a validated specific questionnaire to measure symptoms of PTSD (Impact of Event Scale-Revised), the prevalence of PTSD at 3 months follow-up was 24%, at 6 months 20%, at 12 months 23%, at 24 months 24% [60]. This same study identified baseline depressive illness as the most predictable risk factor for post-ARDS PTSD development. In addition to depression, other identified risk factors included longer length of ICU stay, longer duration of sepsis, and administration of high dose opiates.

Care Provider Contributing Risk Factors

Acknowledging the major impact of specific disease entities upon overall health status and clinical outcomes, in addition multiple care-provider influences have also been demonstrated to assist in paving the pathway to development of CCI. Indeed some factors are clinical that result from disease per se but not surprisingly many factors are personal care-provider mediated and many systems-related. Clinical and treatment factors identified to be major contributors to CCI have included a) inappropriate antibiotic selection, b) fluid overload and electrolyte mismanagement, c) malnutrition, d) excessive sedation, e) hypoglycemia, f) nosocomial infections, g) procedural complications, and h) inappropriate ventilator setting [61]. Although perhaps appearing obvious, this litany of potentially modifiable disease treatment factors again emphasizes the vulnerability of the CCI patient population and the importance of extreme diligence and attention to all management details. Personal care-provider derived negative influences upon CCI patient outcomes that have also been identified include the perceptions that these patients are "unpopular" based upon a) their high care provider dependency, b) long term ICU lengths of stay, c) failure to meet expectations of "genuine" ICU patients, and d) failure to provide challenges or mental stimulation to care providers [62]. Systems problems identified in relation to CCI patients include a) the realization that fewer resources are directed to facilitate chronic care or transfer of care in chronic compared to acute situations, b) after hospital discharge, CCI patients must totally re-enter a new health care system with little effective links between acute and chronic care systems, c) there exists little "ownership" for post-ICU care by the intensivist or critical care physicians initially involved in acute care which by default often falls upon less specifically educated primary care physicians to provide still a remarkably high level of intensive care, and d) the assumption of the majority of post-ICU care provider burden placed upon the patient and family members [63].

Long Term Acute Care Hospitals/Facilities (LTACH) Impact

Acknowledging the potential different treatment and management foci of care teams located at LTACH facilities upon not only continued acute care but also overall rehabilitation and the acute care hospital care-providers upon predominate survival, there still must exist a strong hand-in-hand working relationship between both institutions for optimal patient outcomes. Predominately driven by economic and financial reasons, over the last few decades the care setting for the CCI patients has shifted one-way from acute care hospitals to LTACHs; but

there remains little evidence to suggest that outcomes have improved [15,64]. Multiple studies have repeatedly documented the poor long-term outcomes for patients discharged to LTACHs with one study of 1,414 total LTACH patients transferred specifically for weaning from mechanical ventilation reporting a positive outcome of 54% successful liberation from MV; but the perceived negative outcomes of 25% mortality and 21% persistent ventilator dependency [65]. Another LTACH outcomes study showed that of 133 patients transferred to the LTACH facility; 66 (50%) died at the LTACH and of the 67 (50%) survivors 20 continued to require PMV. Thus from the initial total LTACH admission number of 133, 86 patients or roughly two-thirds of patients transferred to this LTACH had poor outcomes [66]. In addition at one year follow-up, only 30 (23%) were alive, 14% returned home and the remainder were in nursing homes or acute care hospitals, and only 11 (8%) of study patients achieved full independence at one year [66].

Discussion

The attainment of improvement in any specific clinically relevant patient outcome measure involves first, identifying the specific goal(s), second, restructuring thought processes or priorities, and finally active implementation of structured programs to achieve these positive directions.

Defining Positive Outcomes

Appropriately, the majority of ICU- focused comparative therapy outcomes studies focus primarily upon survival. Yet it must also be realized that survival is not the only important outcome measure but consideration of other important factors merit equal emphasis such as functional status, independence, ability to live at home, absence of significant cognitive impairment, and not being a burden to family members physically, socially, mentally, or financially [67]. Thus before attempting to identify pathways to outcomes improvement for CCI patient population, it is first most important to identify those individually- directed patient-specific outcome measures that are deemed most important.

Priority Change

All ICU patients, and especially vulnerable patients, once identified as at risk for CCI progression should receive early and emergent interventions to forestall future suffering, reduced function, necessity for PMV, and prolonged or unsuccessful rehabilitation [15]. Clinical, social, and economical efforts should be accelerated rather than de-escalated as patients' progress to PMV and CCI; realizing that the ultimate care of these CCI patients is as much a societal as medical responsibility.

Institutions, health care systems, critical care providers, and intensivists should assume an intensity of care around the clock, minute by minute, 24 hours per day, 7 days per week to be malleable to the constantly changing dynamics of all aspects of critical illness with requisite staffing, resources and knowledge- based competency to adequately perform this level of clinical care rigor and diligence.

Critical care providers and intensivists should assume leadership roles and increased ownership for CCI patients not only from the perspectives of acute care management but also in relation to long-term recovery and realize that every decision made in the ICU has not only immediate impact but also long-term chronic ramifications measured in days, weeks, months and years.

Critical care providers and intensivists should begin as an early component of ICU care consideration of long-term medical issues and begin both physical and cognitive rehabilitation early in ICU course. This process includes re-focusing therapeutic measures such as early mobilization but also re-organization of the multi-disciplinary ICU care team with inclusion of respiratory therapists, nutritionists, mental health specialists, and physiotherapists integrated as important care-providers.

Critical care providers and intensivists should value objective scales and indices of neurocognitive function, sedation, delirium, and muscle strength and endurance with same validity as standard vital signs.

Critical care providers and intensivists should enter into partnership and "know their LTACHs" to which they transfer or refer patients so as to maintain open avenues of communication and remain in continued ongoing care and overall rehabilitation of the CCI patient to the same rigorous care level as during ICU admission [68].

Within the current knowledge-based limitations for critical care illness prognostication, patients and families should be as best possible educated and informed of potential long-term complications for survivors of acute critical illness.

Finally, critical care providers and intensivists should be aware of the medical, personal, and systems factors that can have major detrimental effects upon the overall health status and quality of life of CCI patients and be prepared to re-set priorities upon recovery and not simply survival.

Conclusion

Although the cumulative detrimental effects of critical illness, ICU-induced malnutrition and immobility, nosocomial complications both infections and procedural, delirium, and prolonged mechanical ventilation have been recognized for decades by critical care physicians and providers, only recently has this population of "chronic critically ill" patients been defined and their negative clinical outcomes in relation to both morbidity and mortality been realized. Potential modifiable risk factors have now been identified which correction may translate into significant clinical benefits for this vulnerable ICU patient population.

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